Introduction

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The content of this supplement is based on the educational symposium entitled ''*Staphylococcal infections – whatever next*?'' which took place at the 15th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) in Copenhagen, April 2005.

Staphylococcus aureus is an important cause of serious infections both in hospitals and the community. This pathogen has overcome almost every attempt to combat it; resistance to a range of antibiotics is widespread among clinical isolates, and methicillin-resistant *S. aureus* (MRSA) is an increasingly common finding. In the last few years, resistance to the conventional first-line agents for MRSA infections, the glycopeptides, has become a worrying reality; the emergence of vancomycin-intermediate strains has been closely followed by a still limited number of fully vancomycin-resistant isolates. At the same time, evidence is building that MRSA is becoming more prevalent, not only in healthcare settings but also within the community – a development that threatens to impact significantly on efforts to control this important pathogen. There is thus a pressing need for new agents to treat *S. aureus* infections, and new drugs, such as the cyclic lipopeptide daptomycin, are welcome additions. This supplement provides a timely analysis of the key issues facing clinicians today, and looks at possible future developments in the battle with this important pathogen.

Professor Gian Carlo Schito sets the scene by briefly reinforcing the importance of *S. aureus* as the cause of serious infections. He discusses the history of the development of antibiotic therapy, and reviews the molecular mechanisms by which *S. aureus* has acquired resistance to many currently available agents. The increasingly widespread use of antibiotics provides the potential for selection of resistant strains through the acquisition of resistance genes. Indeed, multidrug-resistant strains of *S. aureus* are now commonplace across Europe, though the incidence varies significantly among countries. The glycopeptide vancomycin has been considered the mainstay of treatment for drug-resistant *S. aureus* strains for more than 40 years. However, resistance to this antibiotic has now emerged and emphasises the need for new therapies for drug-resistant *S. aureus* infections.

Dr Marjolein Kluytmans-VandenBergh and Dr Jan Kluytmans highlight the emerging problem of community-acquired MRSA (CA-MRSA). Once confined to the hospital environment, MRSA is now emerging as a cause of serious infections in the community. To date, the prevalence of CA-MRSA has been difficult to determine in studies as several definitions of CA-MRSA have been employed. Molecular epidemiological definitions are currently considered to be the most effective method of distinguishing CA-MRSA from hospital-acquired MRSA. The authors also focus on the risk of CA-MRSA strains spreading into hospitals; mathematical models suggest CA-MRSA has the potential to become endemic in both the community and hospital settings. Consequently, the need for measures to contain CA-MRSA is considered to be a matter of urgency.

In the third article, Professor Peter Appelbaum discusses the emergence of vancomycin-intermediate and vancomycin-resistant *S. aureus* strains (VISA and VRSA, respectively) and their impact in the clinical setting. Vancomycin-intermediate isolates were first identified in Japan in 1997 and, more recently, four vancomycin-resistant strains have been identified in the USA. The emergence of such organisms is of considerable concern. Although the precise mechanism of vancomycin resistance has not been determined, a number of studies suggest that thickening of the bacterial cell wall, in addition to other structural and/or metabolic changes involving the cell wall, plays a key role. Directed screening of patients with suspected vancomycin resistance will assist us in establishing the extent of the problem, and be integral to helping us to devise measures to contain it.

The articles in this supplement all emphasise the need for the development of new classes of antimicrobial agents to combat Gram-positive, notably *S. aureus*, infections. Professor Michael Rybak discusses the development of daptomycin, the first in a new class of antibiotics, the cyclic lipopeptides. Daptomycin has a novel mechanism of action, causing depolarisation of the cell membrane, and resulting in bacterial cell death due to widespread disruption of macromolecular synthesis. It is rapidly bactericidal against Gram-positive pathogens, including staphylococci and enterococci. No antagonism has been seen between daptomycin and other antibiotics. In-vitro studies have shown that it is difficult to generate daptomycin-resistant isolates, and the incidence of cross-resistance with existing agents is likely to be low. Daptomycin is indicated in the USA for the treatment of Gram-positive complicated skin and soft tissue infections, and is currently undergoing review by the European Medicines Evaluation Agency (EMEA).

The emergence of resistant *S. aureus* strains is of major clinical concern, and there is an urgent need both for the development of better practice in the use of existing antibiotics, and for novel therapies to treat resistant infections. I hope that the following articles will stimulate further consideration and discussion of possible approaches by which to address the increasing problem of drug-resistant pathogens.